83. (new) The pharmaceutical composition of claim 70, wherein the phospholipid is selected from the group consisting of phosphatidylcholine, phosphatidylglycerol, and mixtures thereof.

B' cancel

84. (new) The pharmaceutical composition of claim 70, wherein the phospholipids are in a liquid crystalline phase at about 37^0C.

REMARKS

The Applicants wish to express their appreciation to Examiner Kishore for the courteous in-person interview held on January 30, 2003. During the interview, the proposed claims which define the liposome compositions used in the invention by their structural properties were discussed. The Applicants note with appreciation the Examiner's indication that such claims, which define the liposomes of the invention as a population characterized by a specific percentage of specifically sized liposomes falling within one standard deviation from the mean, would be favorably considered.

The Claim Amendments

Claims 23-54 have been canceled without prejudice and claims 55-84 have been added. Applicant expressly reserves the right to prosecute any unclaimed or canceled subject matter (including the full scope of any equivalents under the doctrine of equivalents) in any related application. In accordance with the Examiner's suggestions, the Applicant has deleted the terms "preventing" and "managing" from the proposed claims, added a Markush group to define the term "vascular disease" in the proposed claims, and replaced the phrase "not bound to drug" with "free of drug" in the proposed claims which are now incorporated into new claims 55-84.

The new claims are fully supported by the specification and do not constitute new subject matter as defined in 35 U.S.C. § 132. Specifically, claims 55-59 and 70-74 are supported by the originally filed claims and the specification at page 1, lines 23-24; page 4, lines 26-27; page 6, lines 6-25; page 7, lines 28-29; page 7, lines 32-36; page 11, lines 28-29; page 13, line 25; page 13, line 33 to page 14, line 12; page 15, lines 7-23 and page 17, line 26 (disclosing pharmaceutical compositions for the treatment of vascular diseases such as atherosclerosis, hyperlipidemia, and hypoalphalipoproteinemia in humans comprising a pharmaceutically acceptable and therapeutically effective amount of unilamellar phospholipid liposomes free of drug); page 17, lines 8-23 (disclosing liposomes with a diameter of 125 ± 30 nm and 30 ± 7 nm expressed as the mean within plus or minus 1 standard deviation or "S.D."); page 21, line 24 to page 22, line 21; and Figure 4B (showing that liposomes with a mean diameter of 125 ± 30 nm [wherein 68% of the particles are within one standard deviation from the mean] mobilize more cholesterol than an equal amount of unilamellar

liposomes having a mean diameter of 30 ± 7 nm as measured in mice); page 7, lines 25-27; page 8, lines 15-18; and page 17, line 20 (disclosing liposomes having mean diameters between 100-150 nm); and page 8, lines 7-11; page 15, lines 21-22; and page 32, line 25 to page 33, line 32 (disclosing that esterified or LDL cholesterol is not increased and preferably drops during administration of the claimed liposomes). Claims 60-66 and 75-81 are supported by the specification at page 11, line 15 to page 12, line 7 (disclosing specific carriers and specific concentrations of liposomes in the carriers). Claims 67-68 and 82-83 are supported by the specification at page 10, lines 18-35 (disclosing specific phospholipids). Claims 69 and 84 are supported by the specification at page 9, line 7 to page 10, line 11; page 11, lines 6-14; and page 16, line 1 to page 17, line 23 (disclosing phospholipids in a liquid crystalline phase at 37^0C). A copy of the claims that will be pending upon entry of the instant amendment is attached hereto as Exhibit A. The Applicant respectfully requests that the amendments and the addition of new claims herein be entered into the file of the above-identified application and that the remarks herein be fully considered.

In addition, a copy of the Information Disclosure Statement with revised form PTO 1449 submitted to the USPTO on August 9, 2002 is attached hereto as Exhibit G which was requested by the Examiner during the interview on January 30, 2003.

The Claimed Invention

The new claims define the liposome preparation used in the claimed compositions as a "pharmaceutically acceptable and a therapeutically effective amount of unilamellar phospholipid liposomes wherein at least 68% of the liposomes have a mean diameter of 125 ± 30 nm." This is supported by the specification which describes the preparation and use of a population of liposomes having a diameter of 125 nm plus or minus 30 nm as measured by QELS (Quasi-Electric-Light-Scattering) analysis, utilizing a Nicomp Model 370 submicron laser particle sizer (Pacific Scientific, MD) equipped with a 5-mW He-Ne Laser (*see* specification at p. 17, *ll.* 8-23). As explained in the specification, the Nicomp QELS system used to characterize the liposome population analyzes fluctuations in light-scattering intensities due to liposome diffusion in solution. *Id.* The measured diffusion coefficient is used to obtain the average hydrodynamic radius and the mean diameter of liposomes is expressed as the mean plus or minus 1 standard deviation (125 ± 30 nm) (*see* specification at p. 17, *ll.* 8-23), arrived at using a Gaussian analysis (*see, The Nicomp 370 Model Submicron Particle Sizer User Manual* at pp. 24-25, entitled, "The Simplest Approach to Size Distributions: Gaussian Analysis," attached hereto as Exhibit B).[1]

[1] The Nicomp Model 370 automatically selects the appropriate statistical/mathematical procedures to analyze the "raw data" generated by the system (see Exhibit B, p. 24). The Gaussian Analysis, coined as the "simplest approach to size distributions" is the one typically obtained for emulsions prepared by a variety of processes, including sonication, homogenization and microfluidization (see Exhibit B, p. 25).

This analysis uses well-known and accepted mathematical principles to characterize the size distribution of a population, which is expressed as a Gaussian distribution, also known as a "normal" or "bell-shaped" distribution (*see An Introduction to Statistics-Lesson 6: The Bell Shaped, Normal, Gaussian Distribution*, attached hereto as Exhibit C). In a Gaussian, normal, or bell-shaped distribution 68% of the data elements are within one standard deviation of the mean, 95% are within two standard deviations, and 99.7% are within three standard deviations (see Exhibit C, at p. 2, "The Empirical Rule," often stated simply as 68-95-99.7). Thus, the Applicants are claiming a population of liposomes with a very specific Gaussian distribution -- a specific population of liposomes defined by a bell-shaped curve, in which 68% of the population falls within one standard deviation (30 nm) from the mean (125 nm).

A liposome preparation defined by the claims is not disclosed by the prior art and has properties which are surprising and unexpected in view of the teachings of the prior art. Specifically, a population of liposomes wherein at least 68% of the liposomes have a mean diameter of 125 ± 30 nm will surprisingly and unexpectedly mobilize more cholesterol and will control or prevent a rise in LDL and/or esterified cholesterol in contrast to the liposomes disclosed in the prior art (*see* specification at p. 8, *ll.* 7-18; p. 15, *ll.* 21-22; p. 20, *l.* 20 to p. 22, *l.* 21; p. 32, *l.* 25 to p. 33, *l.* 32; and Figures, 2A, 2B, and 4B). *See also* Exhibit D, Rodrigueza et al., *Large Versus Small Unilamellar Vesicles Mediate Reverse Cholesterol Transport In Vivo Into Two Distinct Hepatic Metabolic Pools: Implications For the Treatment of Atherosclerosis,* 17 ARTERIOSCLER. THROMB. VASC. BIOL. (10): 2132-39, 2134 (1997). The prior art describes the administration of smaller liposomes which is associated with significant side effects such as increases in plasma LDL and/or esterified cholesterol levels that can occur after the administration of such liposomes. *See* Figure 2(A) of Williams 1986 which shows that 4 hours after infusion with SUVs (small unilamellar vesicles) there was a dramatic increase in LDL and Figure 5 of Williams 1986 which shows an increase in LDL (peak P1) after SUV treatment. In contrast, LUVs (large unilamellar vesicles) having the claimed Gaussian distribution do not substantially increase LDL or esterified cholesterol and mobilize more cholesterol than SUVs. *See* specification at p. 8, *ll.* 7-18; p. 15, *ll.* 21-22; p. 20, *l.* 20 to p. 22, *l.* 21; p. 32, *l.* 25 to p. 33, *l.* 32; and Figures, 2A, 2B, and 4B. *See also* Figure 2 arrow 2 in Rodrigueza et al., *The Influence of Size and Composition On the Cholesterol Mobilizing Properties Of Liposomes In Vivo*, 1153 BIOCHIMICA BIOPHYSICA ACTA 9-19 (July 1993) (showing no increase in LDL cholesterol after LUV treatment) and Rodrigueza et al., *Cholesterol Mobilization And Regression of Atheroma In Cholesterol-Fed Rabbits Induced By Large Unilamellar Vesicles*, 1368 BIOCHIMICA BIOPHYSICA ACTA 306-320, 312 (col. 2, *ll.* 32-34) (1998) (stating that no changes in esterified cholesterol [CE] plasma concentrations were detected following LUV injections).

Thus, in contrast to the "oceans of liposomes" (as expressed by the Examiner) that may be disclosed by the prior art,[2] the Applicants are claiming a specific and novel population of liposomes defined by their structure and possessing the surprising and unexpected properties of: (1) better cholesterol mobilization and/or, (2) cholesterol mobilization without a substantial increase in LDL or esterified cholesterol levels. The claimed composition was unknown prior to the present invention. For the Examiner's convenience, the Applicants submit herewith a chart summarizing the differences between the claimed invention and the prior art cited by the Examiner in this and related applications, (attached hereto as Exhibit F).

1. The Rejections Under 35 U.S.C. § 102 Should Be Withdrawn

A. The New Claims are Patentable Over Liu

Claims 23-27, 29-32, 34-42, 44-47, and 49-54 were rejected under 35 U.S.C. § 102(b) as being anticipated by Liu (BBA, 1990). According to the Examiner, Liu discloses liposomes having sizes falling within the range claimed by the Applicants (noting the abstract, materials & methods and results of Liu). This rejection is moot since claims 23-54 have been canceled. Nevertheless, Applicants demonstrate below that the newly presented claims are not anticipated by this reference.

Liu does not disclose or suggest a pharmaceutical composition comprising unilamellar phospholipid liposomes: (1) which are pharmaceutically acceptable, (2) in a therapeutically effective amount, (3) that are free of drug, (4) wherein at least 68% of the particles have a mean diameter of about 125 ± 30 nm; and/or (5) which mobilize more cholesterol than an equal amount of unilamellar phospholipid liposomes having a mean diameter of 30 ± 7 nm as measured in mice. Thus, Liu cannot anticipate the pending claims since the Examiner is well aware that anticipation requires identity of the invention. *Akzo N.V. v. International Trade Comm'n*, 808 F2d 1471, 1479-81 (Fed. Cir. 1986). Liu discloses liposomes with an average diameter of less than or equal to 120 nm, or less than or equal to 200 nm; meaning that their size distribution range falls below and outside the Applicant's size distribution range. This is evidenced by the mathematical operator "$\leq$" of Liu (*see e.g.* d $\leq$ 120 & d $\leq$ 200) and the fact that Liu prepares its liposomes by sonication- not by extrusion as in Applicant's invention. Sonication will produce liposomes in the 25-50 nm range. *See* LIPOSOMES 28 (Marc J. Ostro, ed., Marcel Dekker, Inc. 1983). In addition, Liu does not indicate that their liposomes are "pharmaceutically acceptable." In fact, Liu's liposome preparation contains hexadecyl [3H]cholestanyl ether and calcein or ^{125}I-tyraminylinulin and therefore is not "pharmaceutically acceptable."

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[2] Applicants respectfully point out that much of the art that the Examiner is referring to relates to loaded liposomes or liposomes carrying active agents or drugs.

As shown above, Liu does not disclose each and every element of the claimed invention and thus Liu cannot anticipate the claims. At best, Liu describes ranges that may overlap with the range in Applicant's claims but Liu does not disclose a blank liposome (free of drug) that is pharmaceutically acceptable, present in a therapeutically effective amount, and that has the claimed Gaussian distribution with sufficient specificity to constitute anticipation. *Akzo N.V. v. International Trade Comm'n*, 808 F2d 1471, 1479-81 (Fed. Cir. 1986); MPEP 2131.03, entitled "Anticipation of Ranges" ("In order to anticipate the claims, the claimed subject matter must be disclosed with sufficient specificity to constitute an anticipation under the statute."). Thus, Liu does not teach each and every element of the claims, either expressly or inherently, and therefore does not anticipate the claims under 35 U.S.C. § 102(b).

B. The New Claims Are Patentable Over Hager

Claims 23-24, 26-32, 34-47, and 49-54 were rejected under 35 U.S.C. § 102(b) as being anticipated by Hager (EP 0 470 437).[3] According to the Examiner Hager teaches unilamellar liposomes having an average diameter of 129 nm in Example 3 (noting p. 13 of the translation). This rejection is moot since claims 23-54 have been canceled. Nevertheless, Applicants demonstrate below that the newly presented claims are not anticipated by this reference.

Hager does not teach a pharmaceutically acceptable and a therapeutically effective amount of unilamellar phospholipid liposomes wherein at least 68% of the liposomes have a mean diameter of 125 ± 30 nm. Thus, Hager cannot anticipate the pending claims since anticipation requires identity of the invention. *Akzo N.V. v. International Trade Comm'n*, 808 F2d 1471, 1479-81 (Fed. Cir. 1986). At best, Hager describes ranges that may overlap with the range in Applicant's claims but Hager does not disclose a blank liposome suitable for human use that has the claimed Gaussian distribution with sufficient specificity to constitute anticipation.[4] For example in *Akzo N.V. v. International Trade Comm'n*, 808 F2d 1471, 1479-81 (Fed. Cir. 1986) the court held that claims to a process of making aramid fibers using a 98% solution of sulfuric acid were not anticipated by a reference which disclosed using sulfuric acid solution but which did not disclose using a 98% concentrated sulfuric acid solution. *See also* MPEP 2131.03, entitled "Anticipation of Ranges" ("In order to anticipate the claims, the claimed subject matter must be disclosed with sufficient specificity to constitute an anticipation under the statute.").

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[3] U.S. Patent No. 5,741,517 is the English equivalent to EP 0 470 437.

[4] Although Example 3 of Hager discloses liposomes of 129 nm, these liposomes are bound to propidium iodide (a DNA marker that is a known "mutagen" and "irritant,") which is not intended to be administered to a human and not "pharmaceutically acceptable" as required by the claims (*see* Exhibit E, a copy of a Material Safety Data Sheet on propidium iodide from Sigma-Aldrich Corporation; *see also* Aldrich Catalog, p. 1432, 1998-1999). Furthermore, Example 3 does not disclose the Gaussian distribution as claimed.

Thus, because the liposomes of the presently claimed composition are required: (a) to be "pharmaceutically acceptable" (free of propidium iodide, *see* Exhibit E), (b) present in "a therapeutically effective amount," and (c) required to have a particular Gaussian distribution, Hager does not teach each and every element of the claims, either expressly or inherently, and therefore does not anticipate the claims under 35 U.S.C. § 102(b).

2. The Rejections Under 35 U.S.C. § 103(a) Should Be Withdrawn

A. The New Claims are Patentable Over Hager by Itself or in View of Williams 1984 or in Further Combination With Williams 1986 and Konigsberg

Claims 23-32, 34-47, and 49-54 were rejected as obvious over Hager by itself or in view of Williams 1984 (and for claims 33 and 48 in further combination with Williams 1986 and Konigsberg [5,258,499]). This rejection is moot in view of the cancellation of claims 23-54. As discussed below, the new claims define subject matter that is not obvious over the art.

A finding of obviousness requires that the prior art both suggest the invention and provide one of ordinary skill with a reasonable expectation of success. *In re O'Farrell* 853 F2d 894, 903, 7 USPQ2d 1673 (Fed. Cir. 1988). Secondary considerations such as unexpected results must be considered if present. *Stratoflex, Inc. v. Aeroquip Cor*p., 713 F.2d 1530, 1538-39, 218 USPQ 871, 879 (Fed. Cir. 1983); *In re Merck & Co., Inc.*, 800 F.2d 1091, 1096, 231 USPQ 375, 378 (Fed. Cir. 1986). Here, the Applicant's liposome populations having the claimed Gaussian distribution is not suggested by the prior art and achieves unexpected results.

Applicant's unexpected results lie in the discovery that liposomes having the claimed size distribution wherein at least 68% of the liposomes have a mean diameter of 125 ± 30 nm: (1) do not substantially raise LDL or esterified cholesterol levels; and (2) mobilize more cholesterol from peripheral tissues (such as atherosclerotic plaques) than an equivalent amount (per weight) of liposomes having a different Gaussian distribution with smaller liposomes (*see* specification at p. 8, *ll.* 7-18; p. 15, *ll.* 21-22; p. 20, *l.* 20 to p. 22, *l.* 21; p. 32, *l.* 25 to p. 33, *l.* 32; and Figures, 2A, 2B, and 4B). *See also* Figure 2 arrow 2 in Rodrigueza et al., *The Influence of Size and Composition On the Cholesterol Mobilizing Properties Of Liposomes In Vivo*, 1153 BIOCHIMICA BIOPHYSICA ACTA 9-19 (July 1993) (showing no increase in LDL cholesterol after LUV treatment) and Rodrigueza et al., *Cholesterol Mobilization And Regression of Atheroma In Cholesterol-Fed Rabbits Induced By Large Unilamellar Vesicles*, 1368 BIOCHIMICA BIOPHYSICA ACTA 306-320, 312 (col. 2, *ll.* 32-34) (1998) (stating that no changes in esterified cholesterol [CE] plasma concentrations were detected following LUV injections). Liposomes with a size distribution having a smaller mean diameter can cause a substantial rise in LDL or esterified cholesterol levels (bad

cholesterol) which is associated with the development and progression of atherosclerosis; thereby destroying the use of these liposomes for the clinic. *Id.*; *see also* Exhibit D, Applicants post-filing peer reviewed article, Rodrigueza et al., *Large Versus Small Unilamellar Vesicles Mediate Reverse Cholesterol Transport In Vivo Into Two Distinct Hepatic Metabolic Pools: Implications For the Treatment of Atherosclerosis,* 17 ARTERIOSCLER. THROMB. VASC. BIOL. (10): 2132-39, 2134 (1997) (large unilamellar liposomes (123 ± 35 nm) were more efficient in mobilizing unesterified cholesterol than small unilamellar liposomes (34 ± 30 nm), and animals treated with small unilamellar liposomes developed elevated concentrations of esterified cholesterol in contrast to animals treated with liposomes greater than about 123 ± 35 nm which showed no change in esterified cholesterol levels).

Prior to the present invention, only small liposomes (*e.g.*, 21-60 nm) were thought to be useful for the treatment of atherosclerosis. For example, it was generally assumed that the smaller the liposome size, the greater the circulation half-life, and therefore the more cholesterol mobilized (Gregoriadis and Senior, LIFE SCI. 113:183-192 (1986)). It was also expected that smaller liposomes would produce a greater number of HDL-like particles, thus promoting efflux of sterol from peripheral tissues (*see* p. 11, *ll.* 7-20 of the specification citing several prior publications related to this subject). Accordingly, the view prior to the present invention was that small liposomes (*i.e.*, 21-60 nm) were better than larger ones (*i.e.* 123 ± 35 nm). This is a clear teaching away from the claimed invention which contradicts any contention of obviousness.

Hager teaches or suggests the use of small liposomes, particularly when Hager's disclosure as a whole is read in view of the prior art. In fact, Hager teaches using liposomes with a mean diameter as low as 50 nm. Since the prior art as a whole teaches away from using a population of liposomes falling within the claimed Gaussian distribution, the claimed invention is not obvious.

In sum, the claims are not obvious over Hager alone or in combination with any other reference[5] because: (1) the prior art does not suggest pharmaceutically acceptable liposomes in a therapeutically effective amount having the claimed Gaussian distribution; (2) the Applicants have unexpected results showing that liposomes falling within the claimed Gaussian distribution do not substantially raise LDL or esterified cholesterol levels and

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[5] Williams 1984 only discloses liposomes with sizes falling outside the presently claimed size distribution range (*e.g.*, Williams 1984 discloses liposomes with sizes between 21-50 nm and 30-60 nm [p. 419, lines 22-23; p.422, lines 43-45]). Similarly, Williams 1986 discloses liposomes that have been sonicated with a titanium probe for 40 minutes which will produce liposomes with a size distribution in the range of 25-50 nm. *See* LIPOSOMES 28 (Marc J. Ostro, ed., Marcel Dekker, Inc. 1983). Liposomes in the 25-50 nm range are also evidenced by Figures 1 & 2 of Williams 1986 which shows a rise in esterified cholesterol. With respect to Konigsberg (5,258,499), Konigsberg only discloses small unilamellar liposomes that have a mean diameter between 50-100 nm or in ranges that extend below the presently claimed range (down to 30 nm) produced using a probe tip sonicator.

mobilize more cholesterol from peripheral tissues than liposomes falling outside the claimed Gaussian distribution when administered to humans; (3) the prior art teaches away from the invention by emphasizing that liposomes falling outside the claimed Gaussian distribution (*i.e.*, small liposomes of 21-60 nm) are better; and (4) Hager teaches nothing different than the prior art when the prior art is considered as a whole.

B. The New Claims are Patentable Over Williams (1984 or 1986) in view of Liu

Claims 23-27, 28-32, 34-47, and 49-54 were rejected as obvious over Williams (1984 or 1986) in view of Liu. This rejection is moot in view of the cancellation of claims 23-54. The new claims define subject matter that is not obvious over the art for the reasons detailed below.

Williams 1984 or 1986 do not cure the deficiencies of Liu (as discussed in section 1A above) since Williams 1984 or 1986 do not teach or suggest using a population of liposomes falling within the claimed Gaussian distribution. Williams 1984 discloses liposomes with sizes between 21-50 nm and 30-60 nm (p. 419, lines 22-23; p.422, lines 43-45). Similarly, Williams 1986 describes the preparation of SUVs[6] and the uptake of endogenous cholesterol when the SUVs are administered to dogs. The data presented in Williams 1986 shows that 4 hours after infusion with SUVs a dramatic increase in LDL occurs as a result of this treatment (*see* Williams 1986, Fig. 2A, the peak labeled "P1" [LDL] at four hours ["t = 4h"]). Thus, Williams 1986 not only discloses liposomes that are smaller than those presently claimed but the reference actually teaches away from the presently claimed invention because it shows an increase in esterified cholesterol and LDL after administration.

Accordingly, the rejection under 35 USC 103(a) as being unpatentable over Williams (1984 or 1986) in view of Liu should be withdrawn.

C. The New Claims Are Not Obvious Over (Hager By Itself Or In View Of Williams 1984) Or (Williams [1984 Or 1986] In View Of Liu), In Further View Of Barenholz (4,812,314)

Claims 34 and 49 were rejected as obvious over (Hager by itself or in view of Williams 1984) or (Williams [1984 or 1986] in view of Liu), in further view of Barenholz (4,812,314). The Examiner stated that Barenholz is suggestive of the ability of other

[6] In Williams 1986, the phospholipid dispersion was prepared using ultrasonic irradiation (with a titanium probe) for a total of 40 minutes, followed by ultracentrifugation for 1 hour at 100,000 x g to remove fragments of titanium shed by the sonicator probe (*see* Williams 1986 at p. 184, col. 2, last paragraph). This method results in the production of SUVs -- a result confirmed by the data in Williams 1986, Fig. 5 which shows that Williams' SUVs co-elute with the LDL fraction ("P1"), which is known to be 30 nm.

phospholipids to exchange cholesterol through a variety of physiological transfer proteins. However, Barenholz teaches using a suspension of liposomes for treating cellular aging where the liposomes are either multilamellar or contain liposomes below and falling outside our size distribution range. Thus, Barenholz does not remedy the deficiencies noted above with respect to: (1) Hager by itself or Hager in view of Williams 1984, or (2) Williams (1984 or 1986) in view of Liu; and therefore does not make the presently claimed invention obvious.

3. The Rejection Under 35 U.S.C. §112 Second Paragraph, Should Be Withdrawn

The claims were rejected under 35 U.S.C. § 112, second paragraph, for being indefinite.

According to the Examiner, claims 23 and 40 already inherently include a carrier present in the composition such as buffer or water since liposomes are formed by hydration with an aqueous medium. Therefore, the dependent claims which recite "further containing a pharmaceutical carrier" are indefinite (e.g., claims 27 and 42 recite that the pharmaceutical carrier is either water or a buffer). To expedite the prosecution of this application, the Applicant has deleted the dependent claims which recite "further containing" a pharmaceutical carrier.

In addition, the Examiner states that the distinction between saline solution and an aqueous solution containing sodium chloride is unclear and the distinction between buffered water and an aqueous solution containing buffering agents, pH adjusting agents and sodium acetate is unclear. In response, the Applicant respectfully notes that the new claims do not draw such distinctions.

The Examiner also states that since the independent claims recite liposomes "consisting essentially of" phospholipids, claims 34 and 49 which recite non-phospholipids are indefinite and claims 33 and 48 which recite agents bound to the liposomes are indefinite. In response, the Applicant respectfully notes that the new claims use the open ended claim transition term "comprising" to specifically encompass non-phospholipids and other elements.

4. Rejection Under Obviousness-Type Double Patenting

The Examiner has rejected claims 23-54 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,139,871. The Applicant respectfully traverses this rejection in view of the new claims. Alternatively, the Applicant respectfully requests that the Examiner hold this rejection in abeyance until the claims are otherwise deemed allowable at which time the Applicant will file a terminal disclaimer if appropriate based on the final version of the claims allowed.

CONCLUSION

Entry of the foregoing remarks and amendments is respectfully requested. No other fee is believed to be due with this Amendment. However, if any other fee is required, please charge the fee to Pennie & Edmonds LLP Deposit Account No. 16-1150. If any issues remain, the Examiner is requested to telephone the undersigned at (212) 790-9090.

Respectfully submitted,

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Enclosures